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Sociodemographic and Hispanic Acculturation Factors and Isolated Anotia/Microtia

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Abstract

BACKGROUND—It has been observed in several studies that infants with anotia/microtia are more common among Hispanics compared with other racial/ethnic groups. We examined the association between selected Hispanic ethnicity and acculturation factors and anotia/microtia in the National Birth Defects Prevention Study (NBDPS).

METHODS—We examined data from mothers of 351 infants with isolated anotia/microtia and 8,435 unaffected infants from the NBDPS with an expected delivery date from 1997 to 2007. Sociodemographic, maternal, and acculturation factors (e.g. age, maternal education, household income, BMI, gestational diabetes, folic acid, smoking, alcohol intake, study center, parental birthplace and years lived in the United States, maternal language) were assessed as overall risk factors and also as risk factors among subgroups of Hispanics (US- and foreign-born) versus non-Hispanic (NH) whites.

RESULTS—Compared to NH whites, both US- and foreign-born Hispanic mothers demonstrated substantially higher odds of delivering infants with anotia/microtia across nearly all strata of sociodemographic and other maternal factors (adjusted odds ratios (aORs) range: 2.3–8.3). The odds of anotia/microtia was particularly elevated among Hispanic mothers who emigrated from Mexico after age five (aOR=5.67, 95% CI=3.53–9.11) or who conducted the interview in Spanish (aOR=5.72, 95% CI=3.55–9.20).

CONCLUSIONS—We observed that certain sociodemographic and acculturation factors are associated with higher risks of anotia/microtia among offspring of Hispanic mothers.

Keywords

anotia; microtia; acculturation; nativity; Hispanic

INTRODUCTION

Anotia/microtia comprises a spectrum of external ear defects that are present at birth. Microtia is clinically characterized as a small/malformed auricle with or without narrowing or absence of the external auditory canal/meatus (Carey et al., 2006). Anotia constitutes a total absence of the external auricle (Carey et al., 2006). Anotia/microtia can be isolated—

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without an associated defect or identifiable syndrome pattern present (25–45%) (Shaw et al. 2004; Canfield et al., 2009a)—or associated with other birth defects (20–60%) (Kaye et al., 1989; Mastroiacovo et al., 1995; Shaw et al., 2004), most commonly with facial clefts and cardiac defects (Harris et al., 1996). Additionally, across population registry studies, the majority of microtia cases are unilateral (79–93%) (Castilla et al., 1986, Mastroiacovo et al., 1995, Shaw et al., 2004), with the right ear more commonly affected (Klockars et al., 2009). Although a limited number of studies have found some evidence that isolated microtia can be hereditary (Rollnick et al., 1983; Gupta and Patton, 1995; Mastroiacovo et al., 1995; Balci et al., 2001; Klockars et al., 2007), the majority of anotia/microtia cases are considered sporadic—with no family history (Mastroiacovo et al., 1995).

The prevalence of anotia/microtia varies widely across different regions/populations in the US (Suutarla et al., 2007), with estimates in Massachusetts, Texas, California, and Hawaii ranging from 1.0–3.8 per 10,000 births (Shaw et al., 2004; Forrester et al., 2005; Canfield et al., 2009a; Weiss et al., 2009). Both anotia and microtia have been associated with partial or complete reduction in hearing (Carey et al., 2006; Kelley and Scholes, 2007). Compared to children with normal hearing, children diagnosed with hearing loss are also at an increased risk for delayed language development, lower than average reading comprehension, grade failures, and behavioral problems (Bess et al., 1984; Karchmer and Mitchell, 2003; Kelley and Scholes, 2007).

Thalidomide, isotretinoin, and mycophenolate mofetil (an immunosuppressant) have a known teratogenic effect that includes anotia/microtia (Lynberg et al., 1990; Smithells et al., 1992; Anderka et al., 2009). There are numerous chromosomal syndromes associated with ear anomalies, including trisomies 13, 18, and 21 (Mastroiacovo et al., 1995; Shaw et al., 2004) and single gene conditions, such as Treacher Collins and branchiotorenal syndromes, and oculo-auriculo-vertebral spectrum (Gorlin et al., 2001). Outside of known teratogens and recognized genetic conditions, other potential risk factors for anotia/microtia include: advanced maternal age (Harris et al., 1996; Forrester et al., 2005), low maternal educational attainment (Shaw et al., 2004; Zhang et al., 2009), lack of folic acid intake (Ma et al., 2010), insulin-dependent diabetes (Mastroiacovo et al., 1995; Carey et al., 2006; Correa et al., 2008), high parity (Mastroiacovo et al., 1995; Harris et al., 1996), high-altitude geographical areas (Castilla et al., 1986), urban residence (Zhu et al., 2000), and male infant sex (Harris et al., 1996; Canfield et al., 2009a; Paput et al., 2011).

Elevated prevalence rates for anotia/microtia have been reported across different racial/ethnic groups, particularly among Hispanics (Castilla et al., 1986; Harris et al., 1996; Shaw et al., 2004; Yang et al., 2004; Husain et al., 2008; Canfield et al., 2009a), American Indians (Navajo Nation) (Jaffe et al., 1969; Nelson et al., 1984) and Asian/Pacific Islanders (Yang et al., 2004; Forrester et al., 2005). Recently, National Birth Defects Prevention Network (NBDPN) data from selected states (2002–2006) reported a higher prevalence of anotia/microtia in American Indians or Alaskan Natives, Hispanics, and Asian or Pacific Islanders, and a lower prevalence among non-Hispanic black or African Americans as compared to non-Hispanic whites (Population-based Birth Defects Surveillance data from selected states, 2009). Nativity (or place of birth) is an important indicator of ethnic heritage and a multifactorial marker for lifestyle characteristics (e.g., diet, maternal education, smoking,

and alcohol use) and adverse pregnancy outcomes (Scribner and Dwyer, 1989). One recent nativity-focused study found that Hispanic mothers residing in the United States who emigrated from Mexico/Central America were more likely to deliver babies with anotia/microtia compared to US-born Hispanics, regardless of the number of years spent in the United States (Ramadhani et al., 2009). Hispanics in the United States of Mexican heritage share certain similarities that may differ from Hispanics who emigrated from other regions of the world, such as the Caribbean, and thus may contribute to the elevations of anotia/microtia births seen specifically in this population. Many Mexican Americans show genomic evidence of Native American ancestry (Wall et al., 2011). An analysis examining single-nucleotide polymorphisms in the nonrecombining region of the Y-chromosome found the genetic ancestry of the Mexican population to be predominantly European (64.9%), followed by Native American (30.8%) and African (4.2%) (Martinez-Cortes et al., 2012). Alternatively, the various countries found throughout the Caribbean seem to be comprised of a different mixed population. For example, Cuba in their 2002 Census reported the following breakdown of racial groups: White (65.0%), Mulatto (Black and White ancestry) (23.8%), Black (10.1%), and Asian (1.0%) (Central Intelligence Agency, 2008). An understanding of ethnicity, nativity, and the concurrent effect of sociodemographic characteristics is an important step in better understanding the etiology of anotia/microtia.

The National Birth Defects Prevention Study (NBDPS), which has been collecting data since 1997, is the largest study in the United States to look at the causes of birth defects (Yoon et al., 2001). More than 30,000 women selected across ten participating states have been interviewed and provided detailed information on sociodemographic and acculturation factors, as well as an array of other maternal exposures shortly before and during pregnancy. These compiled interview data have given researchers the opportunity to examine defects, such as anotia/microtia, which have been previously difficult to study, and has also provided the unique opportunity to distinguish the occurrence of isolated defects from multiple malformations and syndromes of known etiology (Yoon et al., 2001). While some clues into the etiology of anotia/microtia have been previously explored (as noted above), a great deal of uncertainty continues to exist regarding the factors related to isolated anotia/microtia, particularly among high prevalence groups such as Hispanics (Klockars et al., 2009; Luquetti et al., 2011). This analysis aims to better understand the differences in isolated anotia/microtia observed across Hispanic and non-Hispanic whites in the context of several selected sociodemographic and acculturation factors using NBDPS data.

METHODS

The NBDPS: An Overview

The NBDPS, a large case-control study, was the primary data source used in this analysis. Briefly, the NBDPS was developed to improve the understanding of major structural birth defects by including large, ethnically and geographically diverse birth populations, pathogenetically homogeneous case definitions, and a range of maternal and paternal exposures collected using an extensive computer-assisted telephone interview (CATI) (Yoon et al., 2001). Ten states with ongoing population-based surveillance systems participated in the NBDPS, including Arkansas, California, Iowa, Massachusetts, New Jersey, New York,

Texas, Georgia, North Carolina, and Utah (Yoon et al., 2001). Cases were selected from each state's birth surveillance system and reviewed by Centers' clinical geneticists to establish eligibility using standardized protocols which included the exclusion of all chromosomal and single gene conditions to focus on cases of unknown etiology (Rasmussen et al., 2003). Approximately 30 major birth defects were eligible for inclusion in the study and included the following pregnancy outcomes: live births from all states, fetal deaths (all states except New Jersey and New York), and induced pregnancy terminations (all states except New Jersey, New York, and Massachusetts) (Yoon et al., 2001). Specific criteria for anotia/microtia case selection established by NBDPS clinicians: limited cases to those with microtia type II or more severe. Excluded were microtia type I, a mild structural abnormality without involvement of the external auditory canal, a general description of 'small ear' without description of structural abnormality, and isolated atresia or stenosis of the external auditory canal in the presence of a normal pinna. Isolated cases of microtia were defined using general NBDPS protocols as those cases with just ear abnormalities, or with only the presence of other minor malformations (Rasmussen et al., 2003). NBDPS controls were liveborn infants selected from the same base population as cases with no major malformations and an estimated date of delivery occurring in the same year as cases. Specifically, they were selected from either birth certificates (a random sample of birth certificates based on estimated date of delivery), or birth hospitals (a random sample of unaffected infants from hospital records by month and birth hospital weighted by the number of births per hospital per year) (Cogswell et al., 2009).

Mothers of eligible cases and controls were administered a computer-assisted telephone interview (CATI) taking about one hour in English or Spanish from 6 weeks to 24 months after her estimated due date. Approximately 460 interview questions covered a range of topics including: pregnancy history, maternal disease, tobacco/alcohol/illicit drug use, prescription and over-the-counter medications, preconceptional food intake, maternal/paternal occupations, residence, family history, demographics, stress, and physical activity. Mothers were provided a pregnancy calendar to assist with questions on timing of exposures with the majority of questions, unless otherwise noted, covering the period from three months before conception to the end of pregnancy. The majority of questions were structured with pre-coded response lists, with a few open-ended questions allowing mothers to describe specific chemicals or substances she may have been exposed to (Yoon et al., 2001).

The study protocol was approved in each state by individual institutional review boards.

Study Population: Sample Selected for Analysis

We used NBDPS case and control infants with expected dates of delivery from October 1, 1997 through December 31, 2007. From this version of the data release, we identified 31,827 subjects, of which 507 anotia/microtia cases and all controls (8,494) were selected. Two subjects missing estimated dates of delivery year were excluded from the analyses, as were 147 non-isolated cases (we restricted our analyses to isolated cases to ensure that none of our findings were affected by the presence of other major birth defects). We also excluded 66 subjects diagnosed with type I/II pregestational diabetes mellitus, as a recent

analysis found a positive association between those with type I/II diabetes and isolated anotia/microtia using NBDPS data (Correa et al., 2008).

Statistical Analysis

We conducted a descriptive analysis to determine the distribution of various sociodemographic and acculturation factors among our cases and controls. Statistically significant differences in these factors between cases and controls were assessed using Mantel-Haenszel chi-square tests of statistical independence. To assess the relationship between US- and foreign-born Hispanic ethnicity with anotia/microtia by sociodemographic factors, we examined the association between US- or foreign-born Hispanics and anotia/microtia, using NH whites as the referent category and analysis results stratified by various sociodemographic and acculturation factors detailed in the following 'Variables' section below. Finally, we examined the association between individual Hispanic acculturation and immigration factors and anotia/microtia using five separate Hispanic acculturation groupings adapted from two previous NBDPS analyses (Canfield et al. 2009b; Khodr et al. 2013). A Cochran-Armitage test for trend was conducted on final adjusted models to test for associations across decreasing levels of acculturation for each of the five acculturation groupings. Details on the construction of the individual groupings can also be found in the 'Variables' section below.

Crude and adjusted odds ratios (ORs) and corresponding confidence intervals (CIs) were calculated using logistic regression for each of the models and all analyses were performed using SAS software, version 9.3 (SAS Institute Inc., 2011).

Variables

A range of sociodemographic and acculturation variables were initially considered in our descriptive analysis, including: Hispanic maternal and paternal birthplace (US-, Mexico, and other Foreign-born) and preference of interview language. In addition to consideration in the descriptive analysis above, the following variables were also used in stratified analyses when we examined the association between US- or foreign-born Hispanics and anotia/microtia, using NH whites as the referent category: maternal age at delivery (<25, 25–29, 30–34, 35+ years); maternal education (<12, 12, >12 years completed); pre-pregnancy body mass index (BMI) (underweight, <18.5; normal, 18.5-≤24.9; overweight, 25≤-29.5; or obese, 30+ kilograms per meter squared [kg/m^2]); infant sex (male/female); total annual household income (<$10,000, $10,000-$19,999, $20,000-$39,999, $40,000+); gestational diabetes (Yes/No); maternal alcohol intake one month prior to conception through the third trimester (B1P3); maternal smoking (B1P3); folic acid intake three months prior to conception through the first month of pregnancy (B3P1); family history of anotia/microtia (Yes/No); and study center.

For the Hispanic acculturation and immigration factors analysis, construction of the five separate acculturation groupings included the following individual factors, using NH whites as the referent for each model: 1) *Predominant Language at Home—Hispanic Mothers:* (i.) English; (ii.) Spanish; 2) *Preference of Interview Language—Hispanic Mothers*: (i.) English; (ii.) Spanish, {Preference of language in which the interview was conducted was based on

the interviewer's assessment of the language used for the majority of the interview}; 3) *Years Since Immigration from Mexico—Both Parents Hispanic*: (i.) US-born; (ii.) Mexican-born, 5+ years in the United States; and (iii.) Mexican-born, <5 years in the United States; 4) *Years Since Immigration from Mexico—Hispanic Mothers*: (i.) US-born; (ii.) Mexican-born, 5+ years in the United States; and (iii.) Mexican-born, <5 years in the United States; 5) *Age at Immigration from Mexico—Hispanic Mothers*: (i.) US-born; (ii.) Mexican-born, age of immigration by 5; (iii.) Mexican-born, age of immigration after 5, {Age of immigration was calculated by subtracting the number of years since immigration from maternal age at delivery}. For this part of the analysis, we restricted our sample of foreign-born Hispanic mothers to those born in Mexico. Mothers and fathers born in other Spanish-speaking countries may have created an overly heterogeneous group.

Covariates included in the multivariable logistic regression models based on an a priori decision included: pre-pregnancy BMI, maternal age, maternal education, maternal folic acid supplementation (B3P1), gestational diabetes, maternal smoking or alcohol intake (B1P3), study center, and family history. Family history of anotia/microtia, although also considered to be an important covariate, was rare with only eight subjects, and therefore was not examined further.

Participation among NBDPS anotia/microtia cases and controls for the years 1997–2007 was 70.0% and 65.7%, respectively. Among non-Hispanic (NH) white and Hispanic cases for the same years, participation was 70.4 and 63.6%, and among controls 69.8 and 61.6%, respectively.

RESULTS

We identified 507 cases of anotia/microtia, 360 (71%) of which were isolated, and 8,494 controls in our dataset. After excluding subjects with pregestational type I/II diabetes and those missing estimated date of delivery year, our case and control counts were 351 and 8,435, respectively. A higher percentage of isolated cases of anotia/microtia were Hispanic compared with controls (55.3 and 23.3%, $p<0.01$). Also, a lower percentage of isolated cases were NH black compared with controls, (2.6 and 11.3%, $p<0.01$). Mothers of isolated cases were more likely than controls to report lower education attainment (<12 years) (30.1 versus 17.0%, $p<0.01$), a household income less than $10,000 (27.5 versus 18.8%, $p<0.01$); and among Hispanics, being Mexican-born (55.4 versus 45.3%, $p<0.01$), and speaking Spanish at home (74.6 versus 62.6%, $p<0.01$). Hispanic fathers of isolated cases were also more likely to be Mexican-born (57.8 versus 47.2%, p=0.02) (Table 1).

Compared to NH white mothers, we found statistically significant elevated odds of delivering an infant with anotia/microtia for both US- and foreign-born Hispanic mothers across most of the risk factors assessed, with adjusted ORs (aORs) ranging from 2.3 to 8.3 (Table 2). Particularly noteworthy were the high aORs, with the lower limit of the respective confidence intervals greater than 3.0, for foreign-born Hispanics in the following sociodemographic categories: i.) 25–29 year olds (aOR=6.46, 95%CI=3.13–13.35); ii.) prepregnancy BMI in the obese range (30+ kg/m^2) (aOR=8.27, 95%CI=3.25–21.01); iii.) no folic acid intake (B3P1) (aOR=5.78, 95%CI=3.52–9.50); iv.) reported smoking (B1P3)

(aOR=8.23, 95%CI=3.15–21.48); and v.) no alcohol intake (B1P3) (aOR=5.69, 95%CI=3.58–9.03). Further, among foreign-born Hispanic mothers, considerable differences were noted when comparing strata within the following two groups: 1) maternal education—mothers completing fewer years of education (<12 years) had an aOR more than twice as high as mothers reporting completing more years of education (>12 years) {8.28 versus 3.98}; and 2) prepregnancy BMI—mothers reporting a prepregnancy BMI in the obese range (30+ kg/m^2) had an aOR more than twice as high as the aOR reported in the normal weight range (18.5-≤24.9){8.27 versus 3.69}. Due to small numbers, we were unable to assess differences among the low prepregnancy BMI group (<18.5 kg/m^2) for either the foreign or US-born Hispanic mothers, or examine those reporting gestational diabetes or advanced maternal age (35+) in the US-born Hispanic group (Table 2).

For our Hispanic acculturation and immigration analysis, significantly increased odds were observed in all adjusted estimates for factors assessed among Hispanic parents compared to NH white parents (Table 3). Among Hispanic mothers specifically, we observed increasing risk of anotia/microtia with decreasing acculturation to the US, for maternal language preference and age at immigration. For example, relative to NH whites, the aOR was 2.61 (95% CI=1.66–4.08) for English-speaking Hispanic mothers and 4.86 (95% CI=3.25–7.29) for Spanish-speaking Hispanic mothers. Additionally, among Mexican-born mothers, the aORs were 2.15 (95% CI=0.94–4.91) for those who immigrated by the age of 5 and 5.67 (95% CI=3.53–9.11) for those immigrating after age 5 (Table 3). Cochran-Armitage trend test results were also found to be significant for the factors described above ($p<0.05$, data not shown).

DISCUSSION

This analysis was undertaken to gain a better understanding of the association between sociodemographic factors and Hispanic ethnicity and acculturation and the risk of anotia/microtia. We focused on isolated cases for this analysis to remove the effect of other major defects on the results. Also, by analyzing isolated anotia/microtia, as opposed to anotia/microtia in the presence of other defects, we were able to examine this phenotype as a separate entity with potentially different etiologic and pathogenetic mechanisms underlying its expression (Luquetti et al., 2011). Including other defects, with increased clinical variability, creates the possibility for an overly heterogeneous grouping with the potential to bias our estimates closer to the null. Across nearly all sociodemographic and acculturation factors, we observed substantially increased odds for anotia/microtia among infants born to Hispanic mothers, relative to NH whites. In particular, less-acculturated Hispanic mothers (e.g. those speaking predominantly Spanish or who immigrated to the United States after age 5) had roughly a five-fold increased odds of delivering an infant with isolated anotia/microtia.

Within strata of our selected sociodemographic factors, we found significant aOR elevations of isolated anotia/microtia in both US- and foreign-born Hispanics compared to NH whites. Although many other studies have observed elevations of anotia/microtia among Hispanic mothers compared to NH whites (Harris et al., 1996; Shaw et al., 2004; Yang et al., 2004; Canfield et al., 2009a), foreign-born Hispanics compared to US-born Hispanics (Ramadhani

et al., 2009; Zhu et al., 2006), and Mexican-born Hispanic mothers compared to US-born Hispanics (Canfield et al., 2009a), few studies have looked specifically at these associations restricted to isolated anotia/microtia and stratified by sociodemographic factors. Particularly elevated aORs among low educated and obese US- and foreign-born Hispanic mothers point to the need for further analyses into these specific sociodemographic groups and their association with anotia/microtia.

Additionally, we found that both having the NBDPS interview conducted in Spanish and, in particular, Spanish indicated as the language primarily spoken at home (compared to those indicating English), were both associated with anotia/microtia births. Two recent studies from Texas and California showed a Spanish language association with neural tube defects (Canfield et al., 2009b; Carmichael et al., 2008) among Hispanic mothers. The California analysis looking at markers of acculturation and risk of neural tube defects among Hispanics (Carmichael et al., 2008) found that women with a preference towards speaking Spanish were more likely to have lower education attainment, have lower incomes, and live in areas with higher levels of poverty, and less likely to smoke or drink compared to women indicating a preference for speaking English. Carmichael et al. (2008) noted the growing importance of considering language-based acculturation markers concurrently with other markers such as nativity or time since immigration in the context of birth defects analyses. A mixture of dietary, genetic, and/or other environmental exposures differing between more and less recent immigrants has been postulated in a previous study as playing a role in the underlying etiology of anotia/microtia (Ramadhani et al., 2009).

We also found that regardless of how many years since Mexican-born parents immigrated to the U.S. (<5 or 5+ years), or when they immigrated (by age 5 or after), when compared to NH whites, odds for anotia/microtia remained higher. Time since immigration is a little explored variable and may provide important insight for future studies examining birth defects risk patterns.

Strengths and Limitations

One limitation of this analysis is the possibility of selection bias, which may have been present if a significant number of case mothers who were recent immigrants refused to participate in the study. While participation rates among Hispanics are somewhat lower than non-Hispanic white mothers for the years 1997–2007 at (63.6% versus 70.4%) and (61.6% versus 69.9%) for cases and controls respectively, participation rates by nativity status are not currently compiled by the NBDPS since there are no data on nativity status available for non-participating mothers. Additionally, undocumented immigrant mothers born in Mexico may have underreported their nativity due to concerns about immigration status, although, assuming this underreporting was similar among cases and controls, the misclassification would be non-differential—biasing estimates towards the null.

Another limitation was that clinical data may be collected inconsistently across study centers. Defects defined as ‘microtia’ without other descriptions were included in the study despite the possibility that the term may represent a wide variety of physical manifestations. The possibility exists that some anotia/microtia cases that would not otherwise meet the study inclusion criteria could not be excluded due to limited information from various study

sites. Additionally, computer-assisted interviews were conducted between 6 and 24 months after the expected date of delivery. Among controls, the median time from date of delivery to interview completion was approximately 8 months, and for cases, slightly longer at 11 months. Most of the exposures that we assessed in this study were factors that are easy for the mother to recall such as race, level of education and whether or not she has ever been diagnosed with diabetes. Some exposures, however, such as folic acid and alcohol intake, may have been difficult for some mothers to recall. Assuming case and control mothers had similar issues recalling past exposures, however, misclassification would bias estimates towards the null. The NBDPS minimizes this type of bias by administering the same standard questionnaire to all study participants.

Other limitations of the analysis included our inability to explore the impact of acculturation among other Hispanic subgroups, such as those from Central and South America, due to insufficient sample sizes. Some of these results are therefore generalizable only to Mexican immigrants. Additional important acculturation variables, such as grandparent nativity, social and community support networks, familial assimilation, specific dietary information over extensive periods of time, and religious belief systems, were not collected by the NBDPS, and limited our assessment of acculturation among our Hispanic subgroups. A recent analysis examining ‘familial support’ in foreign versus US-born pregnant Latinas found that higher social support was associated with more positive birth outcomes among foreign-born Latinas only (Campos et al., 2008). The use of a 10-item ‘Familialism Scale’ is presented and may be a useful guide for future analyses on acculturation and birth defects specifically. Additionally, acculturative stress, defined as, ‘reactions to intercultural contact or the cultural adaptation process’ (Berry et al., 2006), including pressures to learn new languages and balancing different cultural values in new environments, may help explain our results. Accurately capturing and further adjusting for an ‘acculturation stress’ proxy variable may have attenuated our findings in the least acculturated groups we examined.

Despite these limitations, using NBDPS data allowed us to include clinically verified and classified diagnoses of a large sample of isolated anotia/microtia cases to examine the degree of acculturation alongside other important risk factors. This analysis also assessed multiple factors for acculturation in Hispanic subgroups while controlling for a range of selected potential risk factors. Number of years since moving to the U.S., in particular, has been examined in previous analyses assessing acculturation and has been found to produce more consistent results than other measures of acculturation, such as more psychometrically defined acculturation constructs including attitudes about ethnic identity, familism, traditionalism, and cultural knowledge (Escobar et al., 2000). In addition, this study allowed for a large, diverse population-based sample of both cases and controls. As Hispanics currently comprise the largest minority group in the US, with the highest birth and immigration rates of any minority group (U.S. Department of Commerce Economics and Statistics Administration, 2007), it is important to continue to examine a variety of co-occurring factors that may lead to the unequal expression of birth defects within this particular ethnic group.

In conclusion, we explored a variety of factors implicated in odds of having an infant with isolated anotia/microtia. As anotia/microtia births appear to be more common in Hispanics

than NH whites, we found that certain sociodemographic and acculturation factors contribute disproportionately to the elevated anotia/microtia births observed among Hispanic parents.

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Table 1

Selected Sociodemographic and Acculturation Factors, Isolated Anotia/Microtia Cases and Controls, National Birth Defects Prevention Study, 1997–2007[a].

	Controls		Cases		
	n	(%)	n	(%)	P (χ^2 test)[c]
Total[b]	**8435**		**351**		
Maternal Race					
Non-Hispanic White	4971	59.0	119	33.9	
Non-Hispanic Black	953	11.3	9	2.6	<0.01
Hispanic	1961	23.3	194	55.3	
Other	547	6.5	29	8.3	
Maternal Age (years)					
<25	2823	33.5	130	37.0	0.73
25–29	2319	27.5	90	25.6	
30–34	2122	25.2	76	21.7	
35+	1171	13.9	55	15.7	
Maternal Education (years)					
<12	1415	17.0	105	30.1	<0.01
12	2000	24.1	87	24.9	
>12	4896	58.9	157	45.0	
Household Income ($)					
<10,000	1407	18.8	86	27.5	<0.01
10,000–19,999	1037	13.9	66	21.1	
20,000–39,999	1833	24.5	78	24.9	
40,000+	3208	42.9	83	26.5	
Infant Sex					
Female	4140	49.1	142	40.5	<0.01
Male	4287	50.9	209	59.5	
Prepregnancy BMI (kg/m^2)					
Underweight (<18.5)	438	5.4	15	4.8	0.22

	Controls		Cases		
	n	(%)	n	(%)	P (χ^2 test)[c]
Normal weight (18.5≤ 24.9)	4455	55.2	166	52.9	
Overweight (25≤ 29.5)	1841	22.8	74	23.6	
Obese (30+)	1335	16.5	59	18.8	
Gestational Diabetes					
Yes	567	6.7	35	10.0	0.02
No	7868	93.3	316	90.0	
Folic Acid Intake (B3P1)[d]					
Yes	4288	51.1	127	36.3	<0.01
No	4100	48.9	223	63.7	
Maternal Smoking (B1P3)[e]					
Yes	1527	18.4	55	15.7	0.20
No	6785	81.6	296	84.3	
Alcohol Intake (B1P3)[e]					
Yes	3067	37.1	109	31.1	0.02
No	5210	63.0	241	68.9	
Study Center					
Arkansas	1064	12.6	25	7.1	
California	1021	12.1	90	25.6	
Iowa	933	11.1	17	4.8	
Massachusetts	1029	12.2	30	8.6	
New Jersey	574	6.8	41	11.7	<0.01
New York	724	8.6	22	6.3	
Texas	996	11.8	67	19.1	
CDC/Atlanta	886	10.5	18	5.1	
North Carolina	594	7.0	12	3.4	
Utah	614	7.3	29	8.3	
Among Hispanics Only	**Controls**		**Cases**		
	1961		**194**		
Language Mother Speaks at Home					

	Controls		Cases		
	n	(%)	n	(%)	P (χ^2 test)[c]
Spanish	1164	62.6	141	74.6	<0.01
English	695	37.4	48	25.4	
Preference of Interview Language[f]					
Spanish	599	31.3	69	35.6	0.23
English	1314	68.7	125	64.4	
Maternal Birthplace					
U.S.	821	43.1	61	31.6	<0.01
Mexico	864	45.3	107	55.4	
Other foreign-born	222	11.6	25	13.0	
Paternal Birthplace					
U.S.	766	40.9	60	31.3	0.02
Mexico	885	47.2	111	57.8	
Other foreign-born	224	11.9	21	10.9	
Among Mexican-born Hispanic Mothers					
Years Mother Lived In US at Time of Interview					
<5	244	33.2	26	27.4	0.71
5+	492	66.8	69	72.6	
Mother's Age at Immigration from Mexico					
≤5	174	20.3	14	13.1	0.08
6+	685	79.7	93	86.9	
Among Mexican-born Hispanic Fathers					
Years Father Lived In US at Time of Interview					
<5	168	22.2	10	10.2	0.01
5+	588	77.8	88	89.8	

[a] Subjects diagnosed with pregestational type I/II diabetes excluded.

[b] Totals for individual characteristics may vary due to missing data.

[c] All p-values reported as two-sided.

[d] During the period from three months prepregnancy through the first month of pregnancy.

[e] During the period from one month prepregnancy through the third month of pregnancy.

[f] As based on the interviewer's assessment of language used for the majority of the interview.

Note: Frequencies for family history not shown due to sparse data.

Table 2

Isolated Anotia/Microtia Among Hispanic and Non-Hispanic Mothers Stratified by Selected Sociodemographic and Acculturation Factors Relative to Non-Hispanic White Parents, National Birth Defects Prevention Study, 1997–2007[a].

	Non-Hispanic White		Hispanic US-Born		Hispanic Foreign-Born	
	Cases/controls	Ref	Cases/controls	aOR (95%CI)[e]	Cases/controls	aOR (95%CI)[e]
Total[b]	**119/4971**		**61/821**		**132/1086**	
Maternal Age (years)						
<25	25/1260	1.0	45/439	**4.45 (2.24–8.83)**	31/308	**5.60 (2.77–11.32)**
25–29	29/1347	1.0	9/208	**2.62 (1.05–6.54)**	29/247	**6.46 (3.13–13.35)**
30–34	34/1435	1.0	6/119	1.03 (0.35–3.05)	22/167	1.83 (0.73–4.54)
35+	27/828	1.0	1/42	*	16/79	**4.38 (1.60–11.96)**
Maternal Education (years)						
<12	5/328	1.0	16/248	**4.36 (1.34–14.20)**	52/387	**8.28 (2.64–25.95)**
12	29/1052	1.0	17/245	**2.35 (1.06–5.24)**	22/224	**4.03 (1.94–8.38)**
>12	81/3490	1.0	28/315	**2.54 (1.42–4.53)**	24/190	**3.98 (2.29–6.91)**
Household Income ($)						
<10,000	12/402	1.0	18/260	1.81 (0.66–4.94)	28/265	**2.83 (1.07–7.52)**
10,000–19,999	14/402	1.0	12/153	1.87 (0.68–5.16)	29/201	**3.35 (1.37–8.21)**
20,000–39,999	33/1149	1.0	13/178	**2.34 (1.00–5.44)**	22/149	**5.06 (2.37–10.80)**
40,000+	53/2542	1.0	9/133	2.32 (0.97–5.60)	6/75	**3.21 (1.25–8.25)**
Infant Sex						
Female	41/2423	1.0	28/382	**2.94 (1.54–5.60)**	42/398	**5.07 (2.85–9.02)**
Male	74/2444	1.0	33/424	**2.36 (1.35–4.14)**	56/402	**4.35 (2.62–7.21)**
Prepregnancy BMI (kg/m^2)						
Underweight (<18.5)	3/255	1.0	6/37	*	4/50	*
Normal weight (18.5≤-24.9)	74/2848	1.0	32/398	**2.75 (1.56–4.85)**	42/406	**3.69 (2.22–6.13)**
Overweight (25≤-29.9)	19/1029	1.0	12/205	1.82 (0.71–4.65)	31/226	**5.17 (2.25–11.92)**
Obese (30+)	19/738	1.0	11/168	**2.98 (1.08–8.20)**	21/119	**8.27 (3.25–21.01)**
Gestational Diabetes						
Yes	6/268	1.0	5/57	*	14/88	**7.98 (1.64–38.89)**

	Non-Hispanic White		Hispanic US-Born		Hispanic Foreign-Born	
	Cases/controls	Ref	Cases/controls	aOR (95%CI)[e]	Cases/controls	aOR (95%CI)[e]
No	109/4602	1.0	56/751	**2.44 (1.57–3.77)**	84/713	**4.43 (3.00–6.54)**
Folic Acid Intake (B3P1)[c]						
Yes	68/3098	1.0	18/258	**2.34 (1.18–4.66)**	21/250	**3.38 (1.78–6.41)**
No	47/1772	1.0	43/550	**2.92 (1.69–5.03)**	77/551	**5.78 (3.52–9.50)**
Maternal Smoking (B1P3)[d]						
Yes	30/1132	1.0	6/115	1.79 (0.58–5.52)	10/39	**8.23 (3.15–21.48)**
No	85/3738	1.0	55/693	**2.74 (1.72–4.35)**	88/762	**4.46 (2.93–6.79)**
Alcohol Intake (B1P3)[d]						
Yes	52/2216	1.0	22/247	**2.52 (1.24–5.15)**	16/157	**3.01 (1.49–6.08)**
No	63/2654	1.0	39/561	**2.82 (1.66–4.80)**	82/644	**5.69 (3.58–9.03)**

[a] Subjects diagnosed with pregestational type I/II diabetes excluded.

[b] Totals for individual characteristics may vary due to missing data.

[c] During the period from three months prepregnancy through the first month of pregnancy.

[d] During the period from one month prepregnancy through the third month of pregnancy.

[e] All models adjusted for the following characteristics (unless the factor has been stratified on): maternal prepregnancy BMI (kg/m^2) (underweight, normal weight, overweight, obese), age (<25, 25–29, 30–34, 35+ years), education (<12, 12, 12+ years), folic acid (3 months before to 1 month after conception), gestational diabetes (Yes/No), smoking (1 month before to 3 months after conception), alcohol intake (1 month before to 3 months after conception) and study center.

* Estimates not reported due to instability in the measure of association.

Note: Estimates for family history and study center not shown due to sparse data.

aOR=adjusted odds ratios; 95%CIs=95% confidence intervals.

Table 3

Adjusted Associations of Isolated Anotia/Microtia with Selected Maternal Acculturation and Immigration Factors for Hispanics Overall and Mexicans, Relative to Non-Hispanic White Parents, NBDPS, 1997–2007[a]

Acculturation/Immigration Factors	Cases		Controls		Adjusted Odds Ratio[b]	95% Confidence Interval
	n	%	n	%		
Total[c]	**351**		**8435**			
Mother and father white, non-Hispanic (Referent for all analyses)	101		4378		1.00	Referent
Predominant Language—Hispanic Mothers						
Predominant language at home is English	48	31.0	688	43.9	**2.61**	**1.66–4.08**
Predominant language at home is Spanish	107	69.0	878	56.1	**4.86**	**3.25–7.29**
Preference of Interview Language[d]—Hispanics Mothers						
Interview language is English	105	66.9	1180	74.8	**3.34**	**2.25–4.97**
Interview language is Spanish	52	33.1	397	25.2	**5.72**	**3.55–9.20**
Years Since Immigration from Mexico—Hispanic Parents						
U.S. Born	40	44.9	449	61.3	**2.77**	**1.58–4.87**
Mexico born, 5+ years in the United States	44	49.4	223	30.4	**6.61**	**3.72–11.76**
Mexico born, <5 years in the United States	5	5.6	61	8.3	**3.08**	**1.10–8.63**
Years Since Immigration from Mexico—Hispanic Mothers						
U.S. Born	61	46.2	808	60.4	**2.71**	**1.70–4.30**
Mexico born, 5+ years in the United States	53	40.2	379	28.3	**5.05**	**3.07–8.31**
Mexico born, <5 years in the United States	18	13.6	151	11.3	**5.05**	**2.65–9.63**
Age at Immigration from Mexico—Hispanic Mothers						
U.S. Born	61	44.2	807	56.8	**2.68**	**1.69–4.25**
Mexico born, Age of immigration by age 5	8	5.8	134	9.4	2.15	0.94–4.91
Mexico born, Age of immigration after age 5	69	50.0	481	33.8	**5.67**	**3.53–9.11**

[a] Subjects diagnosed with pregestational type I/II diabetes excluded.

[b] All models adjusted for the following characteristics: maternal prepregnancy BMI (kg/m2) (underweight, normal weight, overweight, obese), age (<25, 25–29, 30–34, 35+ years), education (<12, 12, 12+ years), folic acid (3 months before to 1 month after conception), gestational diabetes (Yes/No), smoking (1 month before to 3 months after conception), alcohol intake (1 month before to 3 months after conception) and study center.

[c] Totals for individual characteristics may vary due to missing data.

[d] As based on the interviewer's assessment of language used for the majority of the interview.